

That which is claimed is:

1 Isolated nucleic acid encoding a NB-ARC and
5 CARD containing protein (NAC), or functional fragments
thereof, selected from:

(a) ~~DNA encoding the amino acid sequence set forth in SEQ ID NOs:2, 4 or 6, or~~

(b) DNA that hybridizes to the DNA of (a) under moderately stringent conditions, wherein said DNA encodes biologically active NAC, or

(c) DNA degenerate with respect to either (a) or (b) above, wherein said DNA encodes biologically active NAC.

2. A nucleic acid according to claim 1, wherein said nucleic acid hybridizes under high stringency conditions to the NAC coding portion of any of SEQ ID NOs:1, 3 and 5.

3. A nucleic acid according to claim 1, wherein the nucleotide sequence of said nucleic acid is substantially the same as set forth in any of SEQ ID NO:1, 3 and 5.

~~5~~ 4. A nucleic acid according to claim 1, wherein the nucleotide sequence of said nucleic acid is the same as that set forth in any of SEQ ID NOS: 1, 3 and 5.

5. A nucleic acid according to claim 1, wherein
said nucleic acid is cDNA.

6. A vector containing the nucleic acid of claim

7. ~~Recombinant cells containing the nucleic acid of claim 1.~~

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8. An oligonucleotide comprising at least 15
5 nucleotides capable of specifically hybridizing with a
the nucleotide sequence set forth in any of SEQ ID NOs:1,
3 and 5.

9. ~~An oligonucleotide according to claim 8,~~
10 wherein said oligonucleotide is labeled with a detectable
marker.

10. ~~An antisense nucleic acid capable of~~
specifically binding to mRNA encoded by said nucleic acid
15 according to claim 1.

SUB B³ 11. ~~A kit for detecting the presence of the NAC~~
cDNA sequence comprising at least one oligonucleotide
according to claim 9.

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✓ 12. An isolated NAC protein comprising a NB-ARC
domain, a CARD domain and a TIM-Barrel-like domain.

13. The protein of claim 12, further comprising a
25 LRR domain.

14. An isolated protein according to claim 12,
wherein the amino acid sequence of said protein comprises
substantially the same sequence as any of SEQ ID NOs:2, 4
30 or 6.

15. A NAC according to claim 14 comprising the same
amino acid sequence as set forth in any of SEQ ID NOs:2,
4 or 6.

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16. A NAC according to claim 14, wherein said protein is encoded by a nucleotide sequence comprising substantially the same nucleotide sequence as set forth in SEQ ID NOs:1, 3 or 5.

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17. A NAC according to claim 14, wherein said protein is encoded by a nucleotide sequence comprising the same sequence as set forth in SEQ ID NOs:1, 3 or 5.

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18. A method for expression of a NAC protein, said method comprising culturing cells of claim 7 under conditions suitable for expression of said NAC.

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19. An isolated anti-NAC antibody having specific reactivity with a NAC according to claim 12.

20. Antibody according to claim 19, wherein said antibody is a monoclonal antibody.

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21. A cell line producing the monoclonal antibody of claim 20.

22. An antibody according to claim 19, wherein said antibody is a polyclonal antibody.

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23. A composition comprising an amount of the antisense-nucleic acid according to claim 10 effective to inhibit expression of a human NAC and an acceptable hydrophobic carrier capable of passing through a cell membrane.

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24. A transgenic nonhuman mammal expressing exogenous nucleic acid according to claim 1, encoding a NAC.

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25. A transgenic nonhuman mammal according to claim 24, wherein said nucleic acid encoding said NAC has been mutated, and wherein the NAC so expressed is not native NAC.

26. A transgenic nonhuman mammal according to claim 24, wherein the transgenic nonhuman mammal is a mouse.

546 B4, 10 27. A method for identifying nucleic acids encoding a mammalian NAC, said method comprising:

contacting a sample containing nucleic acids with an oligonucleotide according to claim 8, wherein said contacting is effected under high stringency hybridization conditions, and identifying compounds which hybridize thereto.

28. A method for detecting the presence of a human NAC in a sample, said method comprising contacting a test sample with an antibody according to claim 19, detecting the presence of an antibody:NAC complex, and therefor detecting the presence of a human NAC in said test sample.

25 29. Single strand DNA primers for amplification of NAC nucleic acid, wherein said primers comprise a nucleic acid sequence derived from the nucleic acid sequences set forth as SEQ ID NOs:1, 3 and 5.

30 30. A method for modulating the activity of an oncogenic protein, comprising contacting said oncogenic proteins with a substantially pure NAC, or an oncogenic protein-binding fragment thereof.

31. A method of identifying an effective agent that alters the association of a NAC with a NAC associated protein (NAP), comprising the steps of:

5 a) contacting said NAC and NAP proteins, under conditions that allow said NAC and NAP proteins to associate with an agent suspected of being able to alter the association of said NAC and NAP proteins; and

10 b) detecting the altered association of said NAC and NAP proteins, wherein said altered association identifies an effective agent.

15 32. The method of claim 31, wherein said altered association is detected by measuring the transcriptional activity of a reporter gene.

20 33. The method of claim 31, wherein said NAC has nucleotide binding activity.

34. The method of claim 31, wherein said effective agent is a drug.

25 35. The method of claim 31, wherein said effective agent is a protein.

30 36. A method for modulating an activity mediated by a NAC protein, said method comprising:

contacting said NAC protein with an effective, modulating amount of an agent identified by claim 31.

37. The method of claim 36, wherein said modulated activity is selected from the group consisting of: binding of NAC to a CARD-containing protein; binding of NAC to a NB-ARC-containing protein; binding of NAC to a LRR-containing protein; and caspase proteolytic activity.

38. A method of modulating the level apoptosis in a cell, comprising the steps of:

a) introducing a nucleic acid molecule encoding a NAC into the cell; and

b) expressing said NAC in said cell, wherein the expression of said NAC modulates apoptosis in said cell.

39. A method of modulating the level of apoptosis in a cell, comprising introducing an antisense nucleotide sequence into the cell, wherein said antisense nucleotide sequence specifically hybridizes to a nucleic acid molecule encoding a NAC, wherein said hybridization reduces or inhibits the expression of said NAC in said cell.

40. A therapeutic composition comprising a compound selected from a NAC, or functional fragment thereof, a NAC modulating agent identified according to claim 31, or an anti-NAC antibody; and a pharmaceutically acceptable carrier.

41. A method of treating a pathology characterized by abnormal cell proliferation or abnormal inflammation, said method comprising administering an effective amount of the composition according to claim 40.

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42. A method of diagnosing a pathology characterized by an increased or decreased level of a NAC in a subject, comprising the steps of:

5 a) obtaining a test sample from the subject;

b) contacting said test sample with an agent that can bind said NAC under suitable conditions, which allow specific binding of said agent to said NAC;
10 and

c) comparing the amount of said specific binding in said test sample with the amount of specific binding in a control sample, wherein an increased or
15 decreased amount of said specific binding in said test sample as compared to said control sample is diagnostic of a pathology.

43. The method of claim 42, wherein said agent is
20 an anti-NAC antibody or a NAC-associated-protein (NAP).

44. A method of modulating the level of apoptosis in a cell, comprising contacting the cell with an agent that effectively alters the association of NAC with a
25 NAC-associated-protein in the cell, or that effectively alters the activity of a NAC in the cell.

45. A chimeric protein comprising a domain selected from the group consisting of the NB-ARC domain of the NAC
30 of claim 14 and the CARD of the NAC of claim 14.

46. An isolated protein comprising a TIM-Barrel-like domain and a second domain selected from the group consisting of a CARD domain, a NB-ARC domain, and a LRR
35 domain.

47. The chimeric protein of claim 45, comprising the NB-ARC domain of SEQ ID NO:2 and the CARD domain of SEQ ID NO:8.

5 48. The method of claim 31, wherein said agent modulates CARD:CARD association or NB-ARC:NB-ARC association.

10 49. A method of modulating CARD:CARD interactions comprising contacting a NAC protein with the agent of claim 48.

15 50. The method of claim 31, wherein said agent modulates transcription.

51. The method of claim 50, wherein said agent modulates NF- κ B activity.

20 52. A method of modulating transcription comprising contacting a cell with a compound selected from the group consisting of: a NAC protein or functional fragment thereof, an agent identified according to claim 31, and an anti-NAC antibody.

25 53. A method of diagnosing cancer or monitoring cancer therapy comprising contacting a test sample from a patient with the antibody of claim 19.

30 54. A method of assessing prognosis of patients with cancer comprising contacting a test sample from a patient with the antibody of claim 19.

✓
35 55. An effective agent that binds a nucleotide binding site of NAC.

56. An effective agent that modulates the association of NAC or CARD-X with a pro-caspase or a caspase.

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57. The method of claim 56, wherein said pro-caspase is pro-caspase-8 and said caspase is caspase-8.

58. The method of claim 56, wherein said pro-caspase is pro-caspase-9 and said caspase is caspase-9.

59. The method of claim 56, wherein said effective agent inhibits the association of said NAC with said pro-caspase or said caspase.

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60. The method of claim 56, wherein said effective agent increases the association of said NAC with said pro-caspase or said caspase.

61. An effective agent that modulates the association of NAC or CARD-X with a CED-4 family protein.

62. The method of claim 61, wherein said CED-4 family protein is selected from the group consisting of CED-4, Apaf-1, Dark, and CARD4/nod1.

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63. The method of claim 61, wherein said CED-4 family protein is Apaf-1.

64. The method of claim 61, wherein said effective agent inhibits the association of said NAC with said CED-4 family protein.

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65. The method of claim 61, wherein said effective agent increases the association of said NAC with said CED-4 family protein.

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